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(54) Title: NUTRACEUTICAL PRODUCTS CONTAINING SAME AND DIETARY SUPPLEMENTS AND METHOD OF MAN-  
UFACTURING AND USE THEREOF

(57) Abstract: A nutraceutical product comprises a mixture SAME and a dietary supplement, where the moisture content of the  
product is less than 5 weight percent. A nutraceutical preferred product includes a mixture of (RS)-(+)-SAME and (SS)-(+)-SAME  
diastereoisomers, with the (SS)-(+)-SAME diastereoisomer being at a concentration of at least 95 weight percent of the mixture.

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**NUTRACEUTICAL PRODUCTS CONTAINING SAME  
AND DIETARY SUPPLEMENTS & METHOD OF  
MANUFACTURING AND USE THEREOF**

**RELATED APPLICATIONS**

This utility application is based on the following United States provisional patent applications: Serial No. 60/158,298, filed October 8, 1999, entitled Time Release Coated Natural Supplement; Serial No. 60/158,328, filed October 8, 1999, entitled Herbal Mind And Mood Support Composition; Serial No. 60/158,329, filed October 8, 1999, entitled Herbal Stress Support Composition; Serial No. 60/158,480, filed October 8, 1999, entitled Joint Support Composition; and Serial No. 60/158,482, filed October 8, 1999, entitled Herbal Diet And Energy Support Composition. All of these provisional patent applications are incorporated herein by reference and made a part of this application.

**BACKGROUND OF THE INVENTION**

S-adenosyl-L-methionine, and its salts, (either or both herein referred to as SAME) are well known pharmacologically active compositions that combat depression, arthritis, and liver diseases such as, for example, cirrhosis. SAME occurs as two diastereoisomers: (RS)-(+)-SAME and (SS)-(+)-SAME. The (SS)-(+)-SAM-e diastereoisomer is the pharmacologically active diastereoisomer, and SAME products containing (SS)-(+)-SAME at a concentration of at least 95 weight percent (%) of the total diastereoisomers mixture are known. A suitable source of SAME, including the SAME with the higher concentration of the (SS)-(+)-SAME diastereoisomer, is Gnosis S. r. l. of Milan, Italy.

1                                    SUMMARY OF THE INVENTION

2

3            This invention is a nutraceutical product comprising a blend of  
4 SAME and one or more dietary supplements. This nutraceutical product  
5 may be used by both humans and animals. Different nutraceutical  
6 products are provided having multiple beneficial properties. In this  
7 invention the dietary supplements enhance the beneficial effects of the  
8 SAME, or provide additional beneficial effects, or both. The nutraceutical  
9 products of this invention preferably employ SAME with the higher  
10 concentration of the (SS)-(+)-SAME diastereoisomer.

11           The nutraceutical products of this invention may be administered  
12 by any conventional route such as, for example, oral, rectal, nasal,  
13 topical, or parenteral as tablets, caplets, softgel pills, capsules,  
14 suspensions, emulsions, solutions, suppositories, sprays, gums, drops,  
15 lozenges, or injectibles. They may be sold either in bulk to companies  
16 that repackage the product for the consumer or in a form suitable for  
17 use directly by the consumer. For example, if ingested orally, the  
18 nutraceutical products of this invention are in the form of a softgel pill,  
19 caplet, capsule or tablet. Preferably, the softgel pill, caplet, capsule or  
20 tablet is treated with a time release agent. An enteric coating and/or  
21 micro-encapsulation may be employed to achieve time release, and one  
22 suitable time release agent is an aqueous ethyl cellulose dispersion sold  
23 under the trademark Surelease® by Colorcon, Inc. of Santa Ana,  
24 California.

25           Packaging of the nutraceutical products of this invention is  
26 important. As discussed subsequently in greater detail, moisture  
27 adversely affects SAME. Retailers of nutraceutical products usually  
28 conduct accelerated aging tests by subjecting the packaged product to  
29 high temperatures and high humidity over a controlled time duration,  
30 measuring the SAME concentration in the product before and after

1 testing. It has been discovered that the softgel pill, caplet, capsule or  
2 tablet form of the nutraceutical products of this invention completely  
3 enclosed and sealed within an aluminum foil package resist degradation.  
4 Preferably, the softgel pill, caplet, capsule or tablet is first completely  
5 enclosed within a plastic wrap and then completely enclosed and sealed  
6 the aluminum foil. The aluminum foil package acts as a moisture  
7 barrier, enabling said softgel pill, caplet, capsule or table to have  
8 substantially prolonged life when subjected to accelerated testing than a  
9 softgel pill, caplet, capsule or table contained within, for example, a  
10 sealed bottle or plastic blister pack. Preferably, the thickness of the  
11 aluminum foil is from 2 to 6 mils.

12 The nutraceutical products of this invention may also be sold in  
13 forms other than a softgel pill, caplet, capsule or tablet. For example  
14 these products may be used as topical applications such as creams, gels,  
15 patches, etc. They may also be in liquid form especially when used as an  
16 injectibles, or even as an enemas.

17 In the preferred embodiments of this invention the following  
18 dietary supplements are used:

19  
20 Co-Q-10 (Coenzyme Q-10),

21 St. John's Wort derivative, either powder or any form of extract,

22 Ginkgo Biloba derivative, either powder or any form of extract,

23 Ma Huang derivative, either powder or any form of extract,

24 Epimedium pinnatum derivative, either powder or extract,

25 Guarana derivative, either leaf or root powder or any form of

26 extract,

27 Citrus Aurantium derivative, either powder or any form of extract,

28 Kava Kava derivative, either powder or any form of extract,

29 cetyl myristoleate (CMO),

1 cetyl myristoleate blended with cetyl oleate, cetyl esters and cetyl  
2 myristate,  
3 Valerian derivative, either powder or any form of extract,  
4 glutathione,  
5 fructose - 1,6 - diphosphate (FDP),  
6 glucosamine sulfate, glucosamine HCL, or glucosamine potassium,  
7 methyl sulfanyl methane (MSM),  
8 melatonin,  
9 hydrolyzed collagen,  
10 chondroitin sulfate,  
11 citicoline,  
12 alpha GPC.

13  
14 Any one, or combinations of two or more, of these dietary supplements  
15 are mixed with SAME, preferably with the SAME comprising from about  
16 0.1 to about 99 weight percent and the dietary supplement comprising  
17 from about 1 to about 99 weight percent of the nutraceutical product.

18 SAME decomposes in the presence of water and high  
19 temperatures. This presents a problem when blending with dietary  
20 supplements. In accordance with this invention, during manufacture of  
21 the nutraceutical products of this invention conditions are controlled so  
22 that the moisture content of the product is less than 5 weight percent,  
23 preferably less than 3 weight percent. In some instances this may  
24 require drying the dietary supplements prior to blending with the  
25 SAME. In the preferred manufacturing method the SAME and dietary  
26 supplement or supplements being mixed with the SAME are dry  
27 powders having a mesh ranging from about 60 to about 90. The  
28 humidity of the manufacturing environment of nutraceutical product is  
29 less than 25% and the temperature of the manufacturing environment  
30 of nutraceutical product is from 20 to 15 degrees Celsius. The

1 nutraceutical product is encapsulated within capsules within 2 hours  
2 after manufacture. Preferably, these capsules are enteric coated, or  
3 otherwise treat with a time release agent, within 2 hours after  
4 encapsulation.

5 This invention also includes a method of supplementing a diet by  
6 administering for at least 10 to 14 days SAME at a dosage of from 800  
7 to 1200 milligrams per day and at the same time administering a  
8 nutraceutical product comprising SAME and a dietary supplement, said  
9 nutraceutical product including a a dosage of at least 400 milligrams per  
10 day of SAME, and after 14 days administering only said nutraceutical  
11 product.

#### 12 13 DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

#### 14 15 **STRESS REDUCTION COMPOSITION**

16  
17 The preferred stress reduction compositions of this invention  
18 preferably include a combination of SAME and other natural stress  
19 reducing substances in effective amounts for maintaining and/or  
20 improving emotional and physical health during periods of stress. One  
21 preferred embodiment of this invention especially effective in reducing  
22 emotional and physical stress and improving the ability to cope with  
23 such stress is SAME in combination with one or more of the following: a  
24 Kava Kava derivative and a Valerian derivative.

25 The following are the preferred weight percentage ranges of these  
26 stress reduction compositions:

28 <u>Component</u>	<u>Weight Percentage</u>
29 30 SAME	about 5% to about 90%
31 Kava Kava 1-70% Extract Activity	about 5% to about 90%

1 Valerian 1-30% Extract Activity

about 5% to about 90%

2  
3 For efficacy in providing stress reduction, SAME is administered in  
4 dosages ranging from 10 mg to 2000 mg per day. Most preferably,  
5 SAME is present in an amount of 400 mg per total daily dose which is to  
6 be taken one to two times per day. Kava Kava extract is derived  
7 from a tropical plant found in the tropical regions of the Pacific rim and  
8 is known and used for its benefit of relieving symptoms of stress and  
9 anxiety, and to promote and induce relaxation. When used in  
10 combination with SAME, a Kava Kava extract, preferably 1-70% by  
11 weight active ingredient, is present in an amount ranging from 10 mg to  
12 2000 mg per dose per day. Preferably, a 30% by weight active  
13 ingredient Kava Kava extract is present in an amount of 600 mg per  
14 total daily dose taken one to two times.

15 Another composition which is effective in providing health  
16 benefits in the form of stress reduction and/or coping is Valerian  
17 Extract. Valerian is an herbal product known for its anti-anxiety and  
18 stress benefits and is sometimes used to help promote sleep. When used  
19 in combination with SAME, a Valerian Root extract, preferably .8-30%  
20 by weight active ingredient is present in an amount ranging from 10 mg  
21 to 2000 mg per dose per day. Preferably, a 0.8% by weight Valerian  
22 Root extract, is present in an amount of 100 mg per total daily dose  
23 taken one to two times per day.

24 Another preferred composition is to combine all of the above: 200  
25 mg SAME with 600 mg Kava Kava extract, and 100 mg Valerian root  
26 extract within a time-release or enteric coated capsule, caplet, or tablet  
27 along with standard inert ingredients utilized in the art. This  
28 composition to be taken one to two times per day.

Preferred Dosages

1. For the first ten days: Take 800 – 1,200 mg per day of SAME Active Ions– in addition to the Stress Support product.
2. Afterwards, continue only taking the Stress Support product daily.
  - 400 mg of SAME
  - 600 mg of Kava Kava Extract, 30-50% Kavalactones
  - 100 mg Valerian Root Extract (.8 – 1%) Valerenic acid

**WEIGHT REDUCTION AND ENERGY****ENHANCEMENT COMPOSITION**

The preferred weight reduction and energy enhancement compositions of this invention preferably include a combination of SAME and one or more other natural appetite suppressant and/or energy enhancing substances in effective amounts for this purpose. One preferred embodiment of this invention especially effective for weight control and energy enhancement is SAME in combination with one or more of the following: a Ma Huang derivative, a Epimedium Pinnatum derivative, a Citrus Aurantium derivative, and a Guarana derivative. These substances suppress appetite and increase energy. These substances provide weight reduction benefits by speeding up the body's metabolism, thus increasing the body's ability to burn fat without exercise and enhance energy levels.

The following are the preferred weight percentage ranges of these weight reduction and energy enhancement compositions:

<u>Component</u>	<u>Weight Percentage</u>
SAME	about 5% to about 90%
Ma Huang Extract 1-8% Activity	about 5% to about 90%
Epimedium Extract 1-50% Activity	about 5% to about 90%



- 1 Citrus Aurantium Extract 1-40% Activity about 5% to about 90%  
2 Guarana Extract 1-50% Activity about 5% to about 90%

3

4 For efficacy in providing weight loss and energy benefits, SAME is  
5 present in an amount ranging from 10 mg to 2000 mg per day.  
6 Preferably SAME is present in an amount of 400 mg per day two times  
7 per day. Other weight loss benefit compositions may be taken with  
8 SAME.

9 Another composition that is effective in providing health benefits  
10 in the form of weight reduction is Ma Huang. Ma Huang is a naturally  
11 occurring herb which contains as an active weight reduction ingredient  
12 the sympathomimetic compound Ephedra Sinica, or its extract  
13 ephedrine. When used in combination with SAME, Ma Huang Extract,  
14 preferably at a concentration of 1-8% by weight Activity, is present in  
15 an amount ranging from 10 mg to 2000 mg per dose per day.  
16 Preferably, a 6% by weight Ma Huang extract is present in an amount of  
17 300 mg per daily dose taken two times per day before morning and  
18 evening meal.

19 Another composition which is effective in providing health  
20 benefits in the form of weight reduction is Epimedium Pinnatum Extract.  
21 Epimedium Extract is known to increase energy levels and metabolism.  
22 When used in combination with SAME, Epimedium Extract, preferably at  
23 a concentration of 1-50% by weight Activity is present in an amount  
24 ranging from 10 mg to 2000 mg per dose. Preferably, a 10% by weight  
25 Epimedium Pinnatum extract is present in an amount of 100 mg per  
26 daily dose taken two times per day before morning and evening meal.

27 Another composition which is effective in providing health  
28 benefits in the form of weight reduction is Citrus Aurantium Extract.  
29 Citrus Aurantium Extract is known to increase energy levels and  
30 metabolism. When used in combination with SAME, a 1-40% by weight

1 Activity concentration of Citrus Aurantium Extract is present in an  
2 amount ranging from 10 mg to 2000 mg per daily dose. Preferably, a  
3 4% by weight Citrus Aurantium extract is present in an amount of 100  
4 mg per dose taken two times per day before morning and evening meal.

5 Another composition which is effective in providing health  
6 benefits in the form of weight reduction is Guarana Extract. Guarana  
7 Extract is known to increase energy levels and metabolism. When used  
8 in combination with SAME, a 1-50% by weight Activity concentration of  
9 Guarana is present in an amount ranging from 10 mg to 2000 mg daily  
10 per dose. Preferably, a 10% by weight caffeine Guarana extract is  
11 present in an amount of 80 mg per dose taken two times per day.

12 Another preferred composition is to combine all of the above for  
13 an average daily dosage as follows: 200 mg to 400 mg SAME with 900  
14 mg Ma Huang Extract, 200 mg Epimedium Pinnatum Extract, 100 mg  
15 Citrus Aurantium Extract and 100 mg Guarana Extract within a time-  
16 release coated capsule or tablet along with standard inert ingredients  
17 utilized in the art.

18 Another preferred composition is to combine all of the above: 400  
19 mg SAME with 300 mg Ma Huang Extract, 100 mg Epimedium Pinnatum  
20 Extract, 100 mg Citrus Aurantium Extract and 80mg Guarana Extract  
21 within a time-release coated capsule or tablet along with standard inert  
22 ingredients utilized in the art; said composition to be taken two times  
23 per day before morning and evening meal.

#### 24 25 Preferred Dosages

- 26  
27 1. For the first ten days: Take 800 - 1,200 mg per day of SAME  
28 400 mg Active Ions tablets, caplets, or capsules - in addition to  
29 our Diet Support  
30  
31 2. Afterwards, continue only taking the Diet Support composition  
32 daily.  
33

- 400 mg of Active SAME Ions
- 300-400 mg of Ma Huang Extract 6% Alkaloids
- 100 mg Epimedium Pinnatum Extract 10-30% Icariin
- 100-200 mg Citrus Aurantium Extract, 4-6% Synephrine
- 80-120 mg Guarana Seed Extract 10% Caffeine

## JOINT ANTI-INFLAMMATION COMPOSITION

The preferred anti-inflammation compositions of this invention preferably include a combination of SAME and other natural anti-inflammation substances in effective amounts for this purpose. One preferred embodiment of this invention especially effective for inflammation reduction and joint pain is SAME in combination with one or more of the following: methyl sulfanyl methane, cetyl myristoleate, glucosamine sulfate, glucosamine HCL, or glucosamine potassium, and hydrolyzed collagen. These components are known to help (a) relieve symptoms of arthritis and inflammation, (b) rebuild connective tissue, and (c) relieve symptoms related to sport injury and accidents affecting joints. There is a benefit to be found in taking these substances in combination, which increases the overall health benefit to joints over that obtained by taking each substance individually.

The following are the preferred weight percentage ranges of these anti-inflammation compositions:

<u>Component</u>	<u>Weight Percentage</u>
SAME	about 5% to about 90%
methyl sulfanyl methane	about 5% to about 90%
Cetyl myristoleate 1-99% Pure	about 5% to about 90%
Glucosamine sulfate, HCL or potassium	about 5% to about 90%
Hydrolyzed collagen	about 5% to about 90%

1 For efficacy in providing joint health benefits, SAME is  
2 administered in an amount ranging from 10 mg to 2000 mg per day.  
3 Preferably SAME is present in an amount ranging from 400 mg to 800  
4 mg per day. Most preferably, SAME is present in an amount of 100mg  
5 per dose which is to be taken two to three times per day. Other joint  
6 benefit compositions may be taken with SAME.

7 Another composition which is effective in providing health  
8 benefits to joints, is MSM (methyl sulfanyl methane). MSM is known to  
9 reduce symptoms caused by arthritis and sport injuries. When used in  
10 combination with SAME, MSM is present in an amount ranging from 10  
11 mg to 5000 mg per daily dose. Preferably, MSM is present in an  
12 amount of 300 mg per dose taken two times per day.

13 Another composition which is effective in providing health  
14 benefits to joints, is cetyl myristoleate. Cetyl myristoleate is known to  
15 help symptoms of rhumotoid arthritis and inflammation. When used in  
16 combination with SAME, a 1-99% by weight concentration of cetyl  
17 myristoleate is present in an amount ranging from 0.5 mg to 2000 mg  
18 per dose per day. Preferably, an 20% by weight concentration of cetyl  
19 myristoleate is present in an amount of 50 mg per dose taken two  
20 times per day.

21 Another composition which is effective in providing health  
22 benefits to joints is glucosamine sulfate, glucosamine HCL, or  
23 glucosamine potassium. This composition is known to help rebuild  
24 connective tissues and to ease symptoms of arthritis, injury, and  
25 inflammation. When used in combination with SAME, glucosamine  
26 sulfate, glucosamine HCL, or glucosamine potassium is present in an  
27 amount ranging from 10 mg to 2000 mg per dose per day. Preferably,  
28 glucosamine sulfate, glucosamine HCL, or glucosamine potassium is  
29 present in an amount of 1000 mg per dose taken two to three times per  
30 day.

Another preferred composition is to combine all of the above: 100 mg SAME with 300 mg MSM, 50 mg CMO, and 1000 mg glucosamine sulfate within a time-release coated capsule or tablet along with standard inert ingredients utilized in the art; said composition to be taken one to four times per day.

Another preferred composition is to combine all of the above: about 400 mg SAME with about 1000 mg MSM, with about 75 mg cetyl myristoleate, with about 1,000 mg glucosamine sulfate, with about 100 mg hydrolyzed collagen within a time-release coated capsule or tablet.

#### Preferred Dosages

1. For the first ten days: Take 800 – 1,200 mg per day of SAME 400mg Active Ions tablets, caplets, or capsules – in addition to the Joint Support composition
2. Afterwards, continue only the Joint Support daily.
  - 400 mg of Active SAME Ions
  - 1000 – 1,500 mg of Glucosamine Sulfate (or HCL or Potassium)
  - 300-500 mg of MSM (Methylsulfonylmethane)
  - 50-500 mg of CMO blend, 20% Cetyl Myristoleate

#### **MIND AND MOOD ENHANCEMENT COMPOSITION**

The preferred mind and mood enhancement compositions of this invention preferably include a combination of SAME and other natural mind and mood substances in effective amounts for this purpose. One preferred embodiment of this invention especially effective for mind and mood enhancement is SAME in combination with one or more of the following: a St. John's Wort derivative and a Ginko Biloba derivative. These emotional balance and brain function compositions are presented in a variety of formulations, with or without other emotional balance

1 and/or brain function ingredients.

2 According to the invention, the herbal treatment composition  
3 preferably includes the desired combination of natural mood and brain  
4 function promoting substances in effective amounts for maintaining  
5 and/or improving emotional balance and/or memory and/or brain  
6 function. The foregoing descriptions of quantity and dosage are  
7 intended to be specific examples and are not intended to limit the scope  
8 of the invention.

9 The following are the preferred weight percentage ranges of these  
10 mind and mood enhancement compositions:

<u>Component</u>	<u>Weight Percentage</u>
13 SAME	about 5% to about 90%
14 St. John's Wort .1-50%	about 5% to about 90%
15 Ginkgo Biloba 1-99%	about 5% to about 90%

16  
17 For efficacy in providing mind and mood benefits, SAME is  
18 administered in an amount ranging from 10 mg to 2000 mg per day.  
19 Preferably, SAME is used in an amount 400 mg per day. Most  
20 preferably, SAME is used in an amount of 400 mg per daily dose which  
21 is to be taken one to two times per day.

22 Another composition which is effective in providing health  
23 benefits in the form of increased emotional balance is St. John's Wort. St.  
24 John's Wort is a naturally occurring herb which contains the  
25 therapeutically active ingredient hypericin and hyperforin. These  
26 ingredients have an anti-depressive effect which is believed to be  
27 caused by modifying serotonin levels in the brain. When used in  
28 combination with SAME, St John's Wort, preferably a concentration  
29 between .1-50% by weight, is used in an amount ranging from 10 mg to  
30 5000 mg per dose per day. Preferably a 0.3% by weight hypericin

1 concentration of St. John's Wort extract is used in an amount of 900 mg  
2 per daily dose taken two times per day.

3 Another composition that is effective in providing health benefits  
4 in the form of improving memory and brain function as well as acting as  
5 an anti-depressant is Ginko Biloba. When used in combination with  
6 SAME, Ginko Biloba, preferably a concentration between 1-99% by  
7 weight, is used in an amount ranging from 0.5 mg to 2000 mg per dose  
8 per day. Preferably, a 24/6% by weight Ginko Biloba extract, is used in  
9 an amount of 60 mg per daily dose.

10 Another preferred composition is to combine all of the above: 200  
11 to 400 mg SAME with 60 mg Ginko Biloba Extract, and 900 mg St. John's  
12 Wort extract within a time-released coated capsule or tablet along with  
13 standard inert ingredients utilized in the art; said composition to be  
14 taken one to two times per day.

15 Another preferred composition is to combine all of the above:  
16 100mg SAME with 60 mg Ginko Biloba Extract, and 900 mg St. John's  
17 Wort extract within a time-released coated capsule or tablet along with  
18 standard inert ingredients utilized in the art; said composition to be  
19 taken one to two times per day.

20 The present invention may be formulated for administration by  
21 any conventional route including but not limited to oral, rectal, nasal,  
22 topical, or parenteral. The composition may take the form of tablets,  
23 capsules, suspensions, emulsions, solutions, suppositories, sprays or  
24 injectibles, but is not limited to these forms.

#### 25 26 Preferred Dosages

- 27
- 28 1. For the first ten days: Take 800 – 1,200 mg per day of the  
29 SAME 400mg Active Ions tablets, caplets, or capsules – in  
30 addition to our Mind and Mood Product
  - 31
  - 32 2. Afterwards, continue only taking the Mind and Mood  
33 composition daily.

- 400 mg of Active SAME Ions
- 60 mg of Ginkgo Biloba Extract, 24% Flavoneglycosides – 6-7% Terpenelactones
- 500-900 mg of St. John's Wort Extract, .3% Hypericin & 1-2% Hyperforin.

#### **SAME Mind and Mood Support Composition:**

3. For the first ten days: Take 800 – 1,200 mg per day of our SAME 400mg Active Ions tablets, caplets, or capsules – in addition to our Mind and Mood Product
4. Afterwards, continue only taking the Mind and Mood product daily.

- 400 mg of Active SAME Ions
- 60 mg of Ginkgo Biloba Extract, 24% Flavoneglycosides – 6-7% Terpenelactones
- 500-900 mg of St. John's Wort Extract, .3% Hypericin & 1-2% Hyperforin.

#### **LIVER ENHANCEMENT AND ANTI-OXIDANT COMPOSITION**

The preferred liver enhancement and anti-oxidant compositions of this invention preferably include a combination of SAME and other natural liver enhancement and anti-oxidant substances in effective amounts for this purpose. One preferred embodiment of this invention especially effective as a liver enhancement and anti-oxidant is SAME in combination with one or more of the following: Coenzyme Q-10, glutathione, and fructose – 1,6 – diphosphate.

The following are the preferred weight percentage ranges of these liver enhancement and anti-oxidant compositions:

<u>Component</u>	<u>Weight Percentage</u>
SAME	about 5% to about 90%
Coenzyme Q-10	about 5% to about 90%



1	Glutathione	about 5% to about 90%
2	Fructose - 1,6 - diphosphate	about 5% to about 90%

#### Preferred Dosages

- 150 mg Co-Q-10 (Coenzyme Q-10)
- 400 mg SAmE
- 100-300 mg Glutathione
- 50-150 mg Fructose - 1,6 - Diphosphate (FDP)

#### **SAmE Liver and Anti-Oxidant Support**

- 150 mg Co-Q-10 (Coenzyme Q-10)
- 400 mg SAmE
- 100-300 mg Glutathione
- 50-150 mg Fructose - 1,6 - Diphosphate (FDP)

#### **SLEEP ENHANCEMENT COMPOSITION**

The preferred sleep enhancement compositions of this invention preferably include a combination of SAmE and a natural sleep enhancement substances in effective amounts for this purpose. One preferred embodiment of this invention especially effective a sleep enhancement product is SAmE in combination with one or more of the following: melatonin and a Kava Kava derivative.

The following are the preferred weight percentage ranges of these sleep enhancement compositions:

<u>Component</u>	<u>Weight Percentage</u>
SAmE	about 5% to about 90%
Melatonin	about 5% to about 90%
Kava Kava Extract	about 5% to about 90%

Preferred Dosages

- 50 mg Melatonin
- 600 mg Kava Kava Extract, 30% Kavalactones
- 400 mg SAME Active Ions
- 100 mg Valerian Extract .8-1%

The following are examples for the manufacture of the most preferred compositions.

**Production Example I (Stress Reduction Composition)**

**Starting material:**

35.3 kilograms of Kava Kava 30% kavalactones  
47.1 kilograms of SAME, tosylate salt  
5.9 kilograms of Valerian 0.8% by weight Valerenic Acid  
200 kilograms of excipients and miscellaneous fillers  
125,000 "00" size capsules

- Insure that all ingredients are at approximately 2% - 3% moisture content.
- Maintain average humidity of the manufacturing environment at under 25% during manufacture.
- Maintain average temperature of the manufacturing environment is under 20 degrees Celsius.
- Make sure process time from mixture to encapsulation is under 2 hours.
- Within 2 hours of encapsulation, enteric coat , or otherwise treat with a time release agent, the capsules for optimum stability

**Production Example II (Mind and Mood Enhancement Reduction Composition)**

**Starting material:**

50 kilograms of SAME, tosylate salt  
4 kilograms of Ginkgo Biloba Extract 24/6% by weight Extract  
31 kilograms of St. John's Wort, 3% by weight Extract  
240 kilograms of excipients and miscellaneous fillers  
125,000 "00" size capsules

- 1
- 2 • Insure that all ingredients are at approximately 2% - 3% moisture
- 3 content.
- 4 • Maintain average humidity of the manufacturing environment is at
- 5 under 25%
- 6 • Maintain average temperature of the manufacturing environment is
- 7 under 20 degrees Celsius
- 8 • Make sure process time from mixture to encapsulation is under 2
- 9 hours.
- 10 • Within 2 hours of encapsulation, enteric coat, or otherwise treat with
- 11 a time release agent, the capsules for optimum stability
- 12
- 13

#### 14 **Production Example III (Joint Anti-Inflammation Composition)**

##### 15 **Starting material:**

16 33.4 kilograms of SAME, tosylate salt  
17 41.7 kilograms glucosamine sulfate  
18 12.5 kilograms of methyl sulfanyl methane (MSN)  
19 2.1 kilograms of a 20% by weight cetyl myristoleate blend.  
20 10.4 kilograms of excipients and miscellaneous fillers  
21 125,000 "00" size capsules

- 22
- 23
- 24
- 25 • Insure that all ingredients are at approximately 2% - 3% moisture
- 26 content.
- 27 • Maintain average humidity of the manufacturing environment is
- 28 under 25%
- 29 • Maintain average temperature of the manufacturing environment is
- 30 at under 20 degrees Celsius
- 31 • Make sure process time from mixture to encapsulation is under 2
- 32 hours
- 33 • Within 2 hours of encapsulation, enteric coat, or otherwise treat with
- 34 a time release agent, the capsules for optimum stability
- 35

#### 36 **Production Example IV (Weight Reduction and Energy**

#### 37 **Enhancement Composition)**

##### 38 **Starting material:**

39 50 kilograms of SAME, tosylate salt  
40 19 kilograms Ma Huang Extract 6% by weight  
41 6.3 kilograms of Epimedium Pinnatum Extract 10% by weight  
42 6.3 kilograms of Citrus Aurantium Extract 6% by weight  
43 5 kilograms of Guarana Extract 10% by weight  
44  
45

1 13.7 kilograms of excepients and miscellaneous fillers  
2 125,000 "00" size capsules  
3

- 4 • Insure that all ingredients are at approximately 2% - 3% moisture  
5 content.
- 6 • Maintain average humidity of the manufacturing environment is at  
7 under 25%.
- 8 • Maintain average temperature of the manufacturing environment is  
9 under 20 degrees Celsius.
- 10 • Make sure process time from mixture to encapsulation is under 2  
11 hours.
- 12 • Within 2 hours of encapsulation, enteric coat, or otherwise treat with  
13 a time release agent, the capsules for optimum stability  
14  
15  
16

17 **Production Example V (Liver Enhancement and Anti-Oxidant**  
18 **Composition)**  
19

20 **Starting material:**  
21

22 25.8 kilograms of SAME, tosylate salt  
23 9.7 kilograms Co-Q-10  
24 6.5 kilograms glutahion  
25 6.4 kilograms fructose - 1,6 - diphosphate  
26 25.8 kilograms of excepients and miscellaneous fillers  
27 125,000 "00" size capsules  
28

- 29 • Insure that all ingredients are at approximately 2% - 3% moisture  
30 content.
- 31 • Maintain average humidity of the manufacturing environment is at  
32 under 25%.
- 33 • Maintain average temperature of the manufacturing environment is  
34 under 20 degrees Celsius.
- 35 • Make sure process time from mixture to encapsulation is under 2  
36 hours.
- 37 • Within 2 hours of encapsulation, enteric coat, or otherwise treat with  
38 a time release agent, the capsules for optimum stability  
39  
40

41 **Production Example VI (Sleep Enhancement Composition)**  
42

43 **Starting material:**  
44

45 47.1 kilograms of SAME, tosylate salt

- Insure that all ingredients are at approximately 2% - 3% moisture content.
- Maintain average humidity of the manufacturing environment is at under 25%.
- Maintain average temperature of the manufacturing environment is under 20 degrees Celsius.
- Make sure process time from mixture to encapsulation is under 2 hours.
- Within 2 hours of encapsulation, enteric coat, or otherwise treat with a time release agent, the capsules for optimum stability

**SUBSTITUTE SHEET (RULE 26)**

**THE CLAIMS**

1  
2  
3 1. A nutraceutical product comprising a mixture of SAME and Co-Q-  
4 10.

5  
6 2. The nutraceutical product of Claim 1 comprising from 0.1 to 99  
7 weight percent of the SAME and from 1 to 99 weight percent of the Co-  
8 Q-10.

9  
10 3. The nutraceutical product of Claim 2 where the moisture content  
11 of the product is less than 5 weight percent.

12  
13 4. A nutraceutical product comprising a mixture SAME and St. John's  
14 Wort derivative.

15  
16 5. The nutraceutical product of Claim 4 comprising from 0.1 to 99  
17 weight percent of the SAME and from 1 to 99 weight percent of the St.  
18 John's Wort derivative.

19  
20 6. The nutraceutical product of Claim 5 where the moisture content  
21 of the product is less than 5 weight percent.

22  
23 7. A nutraceutical product comprising a mixture SAME and a Ginkgo  
24 Biloba derivative.

25  
26 8. The nutraceutical product of Claim 7 comprising from 0.1 to 99  
27 weight percent of the SAME and from 1 to 99 weight percent of the  
28 Ginkgo Biloba derivative.

1 9. The nutraceutical product of Claim 8 where the moisture content  
2 of the product is less than 5 weight percent.

3

4 10. A nutraceutical product comprising a mixture SAME and a Ma  
5 Huang derivative.

6

7 11. The nutraceutical product of Claim 10 comprising from 0.1 to 99  
8 weight percent of the SAME and from 1 to 99 weight percent of the Ma  
9 Huang derivative.

10

11 12. The nutraceutical product of Claim 11 where the moisture content  
12 of the product is less than 5 weight percent.

13

14 13. A nutraceutical product comprising a mixture SAME and a  
15 Epimedium Pinnatum derivative.

16

17 14. The nutraceutical product of Claim 13 comprising from 0.1 to 99  
18 weight percent of the SAME and from 1 to 99 weight percent of the  
19 Epimedium Pinnatum derivative.

20

21 15. The nutraceutical product of Claim 14 where the moisture content  
22 of the product is less than 5 weight percent.

23

24 16. A nutraceutical product comprising a mixture SAME and a  
25 Guarana derivative.

26

27 17. The nutraceutical product of Claim 16 comprising from 0.1 to 99  
28 weight percent of the SAME and from 1 to 99 weight percent of the  
29 Guarana derivative.

30

1 18. The nutraceutical product of Claim 17 where the moisture content  
2 of the product is less than 5 weight percent.

4 19. A nutraceutical product comprising a mixture SAME and a Citrus  
5 Aurantium derivative.

7 20. The nutraceutical product of Claim 19 comprising from 0.1 to 99  
8 weight percent of the SAME and from 1 to 99 weight percent of the  
9 Citrus Aurantium derivative.

11 21. The nutraceutical product of Claim 20 where the moisture content  
12 of the product is less than 5 weight percent.

14 22. A nutraceutical product comprising a mixture SAME and a Kava  
15 Kava derivative.

17 23. The nutraceutical product of Claim 22 comprising from 0.1 to 99  
18 weight percent of the SAME and from 1 to 99 weight percent of the  
19 Kava Kava derivative.

21 24. The nutraceutical product of Claim 23 where the moisture content  
22 of the product is less than 5 weight percent.

24 25. A nutraceutical product comprising a mixture SAME and cetyl  
25 myristoleate.

27 26. The nutraceutical product of Claim 25 comprising from 0.1 to 99  
28 weight percent of the SAME and from 1 to 99 weight percent of the  
29 cetyl myristoleat .



1 27. The nutraceutical product of Claim 29 where the moisture content  
2 of the product is less than 5 weight percent.

4 28. The nutraceutical product of Claim 27 including cetyl oleate, cetyl  
5 esters, or cetyl myristate.

7 29. The nutraceutical product of Claim 28 comprising from 20 to 80  
8 weight percent of the cetyl myristoleate and comprising from 20 to 80  
9 weight percent of the cetyl oleate, cetyl esters, or cetyl myristate.

11 30. A nutraceutical product comprising a mixture SAME and a  
12 Valerian derivative.

14 31. The nutraceutical product of Claim 33 comprising from 0.1 to 99  
15 weight percent of the SAME and from 1 to 99 weight percent of the  
16 Valerian derivative.

18 32. The nutraceutical product of Claim 31 where the moisture content  
19 of the product is less than 5 weight percent.

21 33. A nutraceutical product comprising a mixture SAME and  
22 glutathione.

24 34. The nutraceutical product of Claim 33 comprising from 0.1 to 99  
25 weight percent of the SAME and from 1 to 99 weight percent of the  
26 glutathione.

28 35. The nutraceutical product of Claim 34 where the moisture content  
29 of the product is less than 5 weight percent.

1 36. A nutraceutical product comprising a mixture SAME and fructose -  
2 1,6-diphosphate.

3  
4 37. The nutraceutical product of Claim 36 comprising from 0.1 to 99  
5 weight percent of the SAME and from 1 to 99 weight percent of the  
6 fructose - 1,6 - diphosphate.

7  
8 38. The nutraceutical product of Claim 37 where the moisture content  
9 of the product is less than 5 weight percent.

10  
11 39. A nutraceutical product comprising a mixture SAME and  
12 glucosamine sulfate, glucosamine HCL or glucosamine potassium.

13  
14 40. The nutraceutical product of Claim 39 comprising from 0.1 to 99  
15 weight percent of the SAME and from 1 to 99 weight percent of the  
16 glucosamine sulfate, HCL or potassium.

17  
18 41. The nutraceutical product of Claim 40 where the moisture content  
19 of the product is less than 5 weight percent.

20  
21 42. A nutraceutical product comprising a mixture SAME and methyl  
22 sulfanyl methane.

23  
24 43. The nutraceutical product of Claim 42 comprising from 0.1 to 99  
25 weight percent of the SAME and from 1 to 99 weight percent of the  
26 methyl sulfanyl methane.

27  
28 44. The nutraceutical product of Claim 43 where the moisture content  
29 of the product is less than 5 weight percent.

1 45. A nutraceutical product comprising a mixture SAME and a dietary  
2 supplement, with the moisture content of the product being less than 5  
3 weight percent.

4  
5 46. The nutraceutical product of Claim 45 where the SAME is a  
6 mixture of (RS)-(+)-SAME and (SS)-(+)-SAME diastereoisomers, with the  
7 (SS)-(+)-SAME diastereoisomer being at a concentration of at least 95  
8 weight percent of the mixture.

9  
10 47. A nutraceutical product comprising a softgel pill, caplet, capsule  
11 or tablet treated with a time release agent, said softgel pill, caplet,  
12 capsule or tablet containing a mixture SAME and a dietary supplement,  
13 with the moisture content of the mixture being less than 5 weight  
14 percent.

15  
16 48. The nutraceutical product of Claim 47 where the softgel pill,  
17 caplet, capsule or table sealed within an aluminum foil package that acts  
18 as a moisture barrier, enabling said softgel pill, caplet, capsule or tablet  
19 to have substantially prolonged life when subjected to accelerated  
20 testing than a softgel pill, caplet, capsule or table contained within a  
21 sealed bottle.

22  
23 49. The nutraceutical product of Claim 47 where the time release  
24 agent is an aqueous ethyl cellulose dispersion.

25  
26 50. The nutraceutical product of Claim 47 where the SAME is a  
27 mixture of (RS)-(+)-SAME and (SS)-(+)-SAME diastereoisomers, with the  
28 (SS)-(+)-SAME diastereoisomer being at a concentration of at least 95  
29 weight percent of the mixture.

1 51. A nutraceutical product comprising a mixture of SAME, a Kava  
2 Kava derivative, and a Valerian derivative.

3

4 52. The nutraceutical product of Claim 51 where the Kava Kava  
5 derivative includes from 30 to 50 weight percent Kavalactones.

6

7 53. The nutraceutical product of Claim 51 where the Valerian  
8 derivative includes from 0.8 to 1 weight percent Valerenic acid.

9

10 54. A nutraceutical product comprising a mixture of SAME, a Ginkgo  
11 Biloba derivative, and a St. John's Wort derivative.

12

13 54. A nutraceutical product comprising a mixture of SAME,  
14 glucosamine sulfate, methyl sulfanyl methane, and cetyl myristoleate.

15

16 55. A nutraceutical product comprising a mixture of SAME, Ma Huang  
17 derivative, Epimedium Pinnatum, derivative, Citrus Aurantium  
18 derivative, Guarana derivative.

19

20 56. A nutraceutical product comprising a mixture of SAME, Co-Q-10,  
21 glutathion, and fructose - 1,6 - diphosphate.

22

23 57. A nutraceutical product comprising a mixture of SAME, a Kava  
24 Kava derivative, a Valerian derivative, and melatonin.

25

26 58. A nutraceutical product comprising a mixture of SAME and at least  
27 two of the following ingredients:

28

Co-Q-10 (Coenzyme Q-10),

29

St. John's Wort derivative, either powder or any form of extract,

30

Ginkgo Biloba derivative, either powder or any form of extract,

1 Ma Huang derivative, either powder or any form of extract,  
2 Epimedium pinnatum derivative, either powder or extract,  
3 Guarana derivative, either leaf or root powder or any form of  
4 extract,  
5 Citrus Aurantium derivative, either powder or any form of extract,  
6 Kava Kava derivative, either powder or any form of extract,  
7 cetyl myristoleate (CMO),  
8 cetyl myristoleate blended with cetyl oleate, cetyl esters and cetyl  
9 myristate,  
10 Valerian derivative, either powder or any form of extract,  
11 glutathione,  
12 fructose - 1,6 - diphosphate (FDP),  
13 glucosamine sulfate, glucosamine HCL, or glucosamine potassium,  
14 methyl sulfanyl methane (MSM),  
15 melatonin,  
16 hydrolyzed collagen,  
17 chondroitin sulfate,  
18 citicoline,  
19 alpha GPC.

20  
21 57. A nutraceutical product comprising a mixture of SAME and  
22 melatonin.

23  
24 58. A nutraceutical product comprising a mixture of SAME and  
25 hydrolyzed collagen.

26  
27 59. A nutraceutical product comprising a mixture of SAME and  
28 chondroitin sulfate,

29 60. A nutraceutical product comprising a mixture of SAME and  
30 citicoline,

1 61. A nutraceutical product comprising a mixture of SAME and alpha  
2 GPC.

3  
4 62. A method of manufacturing a nutraceutical product comprising  
5 mixing SAME and a dietary supplement under conditions where the  
6 moisture content of the product is less than 5 weight percent.

7  
8 63. The method of Claim 62 where the humidity of the manufacturing  
9 environment of nutraceutical product is less than 25%.

10  
11 64. The method of Claim 62 where the temperature of the  
12 manufacturing environment of nutraceutical product is from 20 to 15  
13 degrees Celsius.

14  
15 65. The method of Claim 64 where the nutraceutical product is  
16 encapsulated with capsules within 2 hours after manufacture.

17  
18 66. The method of Claim 65 where the capsules are enteric coat, or  
19 otherwise treat with a time release agent, within 2 hours after  
20 encapsulation.

21  
22 67. A method of supplementing a diet by administering for at least 10  
23 to 14 days SAME at a dosage of from 800 to 1200 milligrams per day  
24 and at the same time administering a nutraceutical product comprising  
25 SAME and a dietary supplement, said nutraceutical product including a  
26 dosage of at least 400 milligrams per day of SAME, and after 14 days  
27 administering only said nutraceutical product.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/27559**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : A61K 31/12, 31/20, 31/40, 31/66, 31/70, 35/78, 39/385

US CL : 424/195.1, 514/ 46, 125, 415, 560, 689

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/195.1, 514/ 46, 125, 415, 560, 689

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
REGISTRY, CAPLUS, NAPRALERT, BIOSIS, MEDLINE, EMBASE, WPIDS**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Database CAPLUS on STN (Columbus, OH, USA), No. 129:347310, HENDERSON ET EL. 'Amino sugar, glycosaminoglycan or glycosaminoglycan-like compounds, and S-adenosylmethionine,' abstract, WO 9848816 A1, 19981105.	1-67
Y	Database CAPLUS on STN, (columbus, OH, USA), No. 130:329206, HENRIKSEN, B 'Pharmaceutical formulation for treating liver disorders containin inorganic selenium and vitamins,' abstract, EP 913155 A2, 19990506.	1-67

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*E* earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*A* document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

14 DECEMBER 2000

Date of mailing of the international search report

17 JAN 2001

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